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Original Research

Pre-Operative Parameters Predicting Hemoglobin Decline Related to Percutaneous Nephrolithotomy

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Abstract

Objectives: Percutaneous nephrolithotomy (PNL) for upper urinary tract stones is a minimally invasive, effective treatment modality. Despite its high success rates, its potential complications pose a risk. In this study, we aimed to determine the risk factors associated with bleeding which is one of PNL's most important complications.

Methods: The data of patients who underwent PNL between January 2017 and December 2018 were retrospectively analyzed. The median reduction in post-operative hemoglobin levels compared to preoperative levels was found to be 1.6 g/dl, which was accepted as the threshold value. The patients with hemoglobin decrease above the threshold were assigned as Group 1, and below the threshold as Group 2. Pre-operative, perioperative data, and stone characteristics of the patients were recorded.

Results: 169 patients, 85 patients in Group 1 and 84 patients in Group 2 were included in the study. The mean age of Group 1 was significantly higher (47.4±7.9 and 32±9.4 years, respectively, p=0.001) Sixteen in Group 1 (18.8%) and six in Group 2 (7, 1%) had a diagnosis of hypertension (HT) and a significant difference was found (p=0.038). The average stone burden was 2733±1121.3 mm3 in Group 1, and 2326.5±975.6 mm^3 in Group 2. It was observed that there was a significantly higher stone burden in Group 1 (p=0.001). There was a significant difference between the groups in terms of mean operation time (84.4±7 and 76.2±9.9 min, respectively, p<0.001). When the complication rates were analyzed, complications were observed in 25 (29.4%) patients in Group 1 and 12 (14.2%) patients in Group 2, and a significant difference was found between both groups (p=0.019). Age and HT were found to be significant independent risk factors associated with hemoglobin decline in multivariate analyzes (p<0.001 and p<0.027, respectively).

Conclusion: In this study; advanced age, presence of HT, and high stone burden were found to be predictive of reductions in hemoglobin levels. Furthermore, a correlation of decreased hemoglobin levels was detected with operative times and occurrence of complications.

Keywords: Hemorrhage, kidney calculi, percutaneous nephrolithotomy

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Percutaneous nephrolithotomy (PNL) for the upper urinary tract stones is a minimally invasive, repeatable, and effective treatment modality.[1] Indications for PNL were determined as the presence of larger than 2-cm-stones in the upper urinary tract or the presence of larger than 1.5-cm-lower pole stones resistant to extracorporeal

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shock wave lithotripsy.[2] Success rates of higher than 90% have been reported in the literature.[1] However, complications such as acute injuries to the collecting system and adjacent organs, infections, and prolonged urinary leakage can occur at rates of up to 25%.[3] Post-PNL bleeding is still a common and serious complication. Although conservative treatment is sufficient in most cases, selective arterioembolization is required in 0.8% of the cases.[4]

The previous studies have shown that diabetes mellitus (DM), hypertension (HT), urinary tract infections, staghorn stones, and the number of access are associated with post-PNL hemorrhage.[5-7] There will be significant improvements in morbidity and mortality rates by determining the risk factors associated with bleeding and individualizing the perioperative and post-operative processes in the light of these factors. In this study, we aimed to determine the factors predicting decreased post-operative hemoglobin levels in patients undergoing PNL.

Methods

On receiving the ethics committee approval; patients, who underwent PNL in Bakırkoy Dr. Sadi Konuk Training and Research Hospital in the period between January 2017 and December 2018, were retrospectively analyzed (2021/06). Patients with anatomical or functional anomalies in the urinary system; patients, who underwent other surgical procedures or bilateral surgery in the same session; patients with multiple access performed, and patients with chronic renal failure were not included in the study to have a homogeneous group of patients. Patients with complete staghorn stones were also excluded from the study because it was thought to create heterogeneity in the measurement of stone volume and parenchymal thickness.

Patients were examined preoperatively by contrast-enhanced computed tomography (CT) or intravenous pyelography. Samples for urine culture tests were collected from each patient preoperatively. Patients with positive urine culture test results were treated with appropriate antibiotherapy. Intravenous prophylactic therapy with second generation cephalosporins was administered to all patients preoperatively. Before access, an ipsilateral ureteral catheter was inserted in all patients in the lithotomy position. Then, fluoroscopic access was achieved while the patients were lying in the prone position. The tract was expanded with a high-pressure balloon dilator up to 18 atm and a 30 F Amplatz sheath was placed on it. Using a 24 Fr nephroscope (Karl Storz GmbH and Co. KG, Tuttlingen, Germany), stones were fragmented by means of a pneumatic lithotripter (Vibrolith®, Elmed, Ankara, Türkiye), and stones were extracted using forceps. In the majority of the cases, a 20-22F nephrostomy catheter was placed in the renal pelvis or the respective calyx. When no residual renal stone fragments remained, nephrostomy catheters were removed postoperatively in the 24th h. The stone-free status of the patients was evaluated by direct urinary system radiography in the early post-operative period and by low-dose non-contrast whole abdominal CT in the 3rd month after surgery.

Hemoglobin levels of all patients were tested 1 week before the surgery through complete blood counts. The median reduction in post-operative hemoglobin levels compared to pre-operative levels was found to be 1.6 g/dl, which was accepted as the threshold value. Patients were divided into two groups based on the threshold value. Patients with reductions in hemoglobin levels by more than 1.6 g/dl were assigned to Group 1 and patients with reductions by less than the threshold value were assigned to Group 2. Preoperative and perioperative patient data were recorded including age, gender, body mass index (BMI), comorbid diseases (HT, DM), American Society of Anesthesiologists (ASA) scores, Charlson Comorbidity Index (CCI) scores, operative times, erythrocyte replacement therapy (ERT), the length of hospital stay, and complications. Operative time was defined as the time elapsed from insertion of the ureteral catheter to the completion of the lithotripsy and the insertion of the nephrostomy catheter. The side of the intervention for the stones, stone burden, the mean Hounsfield Unit (HU) value, the grade of hydronephrosis; S.T.O.N.E,[8] Clinical Research Office of the Endourological Society (CROES),[9] and GUY'S[10] nephrolithotomy scores, and rates of postoperative stone-free status were recorded. Pre-operative total stone volumes (cm^3) were calculated using the length × height × width × π × 1/6 formula and axial images obtained by coronal reconstructions of non-contrast CT scans.[11] Stones larger than 4 mm were defined as residual stones. Complications were classified according to the Clavien-Dindo system.[12]

Statistical Analysis

Categorical data were given as numbers and percentages. Means and standard deviations were calculated for continuous variables. The normal distribution of the continuous variables was tested by the Kolmogorov–Smirnov test. Means of two normally distributed groups were compared using Student's t-test. The frequency of categorical variables was compared using Pearson Chi-square test. The $p<0.05$ was regarded as statistically significant. Univariable and multivariable binary logistic regression analyses were used to identify the predictive factors of hemoglobin decrease. The receiver operating curve (ROC) analysis was performed to measure the model's predictive power. Statistical analysis was performed using Statistical Package for the Social Sciences version 21 (IBM SPSS Statistics; IBM Corp., Armonk, NY).

Results

Data of 169 patients were analyzed retrospectively after the inclusion and exclusion criteria were applied. There were 85 patients in Group 1 and 84 patients in Group 2. Demographic data and the pre-operative and perioperative data of the patients are presented in Table 1. When the groups were compared, it was observed that the mean age of the patients in Group 1 was significantly higher compared to the mean age of the patients in Group 2 (p=0.001). Statistical analyses revealed no significant changes in gender, BMI, CCI, and ASA scores between the groups. DM and HT were examined separately as comorbidities. There were 9 (10.5%) patients with DM and 16 (18.8%) patients with HT in Group 1 and there were 13 (15.4%) patients with DM and 6 (7.1%) patients with HT in Group 2. It was observed that concomitant HT diagnosis was significantly higher in Group 1 (p=0.038).

Considering all patients included in the study, 59.2% of stones were located on the right and 40.8% were located on the left. The mean HU was 999.1±319.3 in Group 1 and 960.2±306.5 in Group 2. There were no significant differences in neither variable between the groups. The mean stone burden was found to be 2733±1121.3 mm^3 in Group 1 and 2326.5±975.6 mm^3 in Group 2. Group 1 had a significantly higher stone burden (p=0.001). No significant differences were observed in hydronephrosis, the skin-to-stone distance, skin-to-kidney distance, and S.T.O.N.E, CROES, GUY's nephrolithotomy scores between the two groups (p<0.005). The variables about the stone characteristics are shown in Table 2.

When all patients were evaluated, it was found that 6.4% had preoperative nephrostomy and 4.1% had a preoperative ureteral catheter. The rate of previous open stone surgery was 8% and the rate of previous endoscopic stone surgery was 27.6%. There

were no significant differences in the history of the placement of pre-operative catheters and previous stone surgery between the two groups.

A significant difference in operative times was found between the groups (84.4±7 min and 76.2±9.9 min, respectively; p<0.001). The length of stay in the hospital was not significantly different between the groups. When complication rates were analyzed, it was observed that complications occurred in 25 (29.4%) patients in Group 1 and in 12 (14.2%) patients in Group 2. As expected, more complications were recorded in the group with higher hemoglobin decrease, and a significant difference was found between both groups (p=0.019). In Group 1, two Clavien 3b complications occurred, which were selective arterioembolization procedures under general anesthesia due to bleeding. In Group 2, the only Clavien 3b complication was ureteral stent placement under general anesthesia due to partial

Table 1. Patients demographics, peroperative, and post-operative datas

Parameters (mean±SD)	Total (n=169)	Group 1 (n=85)	Group 2 (n=84)	P
Decrease in Hg (g/dl)	1.9±0.6	2.8±1.2	0.8±0.4	0.001
Age (year)	39.7±11.5	47.4±7.9	32±9.4	0.000
Gender (m/f) (n; %)	130/39 (76.9/23.1)	64/21 (75.3/24.7)	66/18 (78.6/21.4)	0.374+
Comorbidities				
DM (n; %)	22 (13)	9 (10.5)	13 (15.4)	0.370
HT (n; %)	22 (13)	16 (18.8)	6 (7.1)	0.038
BMI (kg/m^2)	27.4±3.1	27.2±2.8	27.5±3.4	0.584
Operation time (min)	80.2±10	84.4±7	76.2±9.9	0.000
LOS (day)	3.6±1.5	3.7±1.7	3.4±1.3	0.217
Complication (n; %)	37 (21.8)	25 (29.4)	12 (14.2)	0.019+
Clavien 1	9 (5.3)	4 (4.7)	5 (5.9)	
Clavien 2	16 (9.46)	13 (15.2)	3 (3.5)	
Clavien 3a	9 (5.3)	6 (7)	3 (3.5)	
Clavien 3b	3 (1.7)	2 (2.3)	1 (1.1)	
ERT (n; %)	11 (6.5)	11 (12.9)	0 (0)	0.001+
SFR (n; %)	136 (80.4)	66 (77.6)	70 (83.3)	0.351

SD: Standard deviation; Hg: Hemoglobin; DM: Diabetes mellitus; HT: Hypertension; BMI: Body mass index; LOS: Length of stay; ERT: Erythrocyte replacement therapy; SFR: Stone free rate.

Table 2. Stone characteristics

	Total (n=169)	Group 1 (n=85)	Group 2 (n=84)	P
Laterality (n; %)				
Left	69 (40.8)	33 (38.8)	36 (42.9)	0.353+
Right	100 (59.2)	52 (61.2)	48 (57.1)	
Stone Burden (mean±SD)	2530.9±1067.9	2733±1121.3	2326.5±975.6	0.013
HU (mean±SD)	979.8±319.3	999.1±332.2	960.2±306.5	0.431
Hydronephrosis (n; %)				
0	18 (10.7)	8 (9.4)	10 (11.9)	0.234+
1	61 (36.1)	31 (36.5)	30 (35.7)	
2	67 (39.6)	34 (40)	33 (39.3)	
3	19 (11.2)	12 (14.1)	7 (8.3)	
4	4 (2.4)	-	4 (4.8)	
S.T.O.N.E	7.4±1.6	7.64±1.6	7.2±1.6	0.153
CROES	196.4±62.6	190.5±64.1	202.4±60.8	0.216
GUY'S				
1	55 (32.5)	28	27	0.556+
2	69 (40.8)	31	38	
3	24 (14.2)	13	11	
4	21 (12.4)	13	8	

SD: Standard deviation; HU: Hounsfield Unit; CROES: Clinical Research Office of the Endourological Society.

ureter rupture. A total of nine Clavien 3a complications were observed; six were ureteral stent placement under local anesthesia due to fragmentation or clot formation, one was the placement of an intercostal drainage tube under local anesthesia for pneumothorax, one was sepsis that improved with supportive treatment and antibiotic therapy, and one was the long-term retention of the nephrostomy catheter due to pelvis perforation.

Following PNL, 11 (6.5%) patients received ERT. All of these patients were in Group 1 and there was a significant difference in receiving ERT between the two groups (p=0.001). When the postoperative stone-free rates were examined, it was found that 83.3% of the patients were stone-free in Group 2 and this rate was higher than the rate observed in Group 1 (77.6%). However, statistical analysis showed no significant difference between the groups in terms of postoperative stone-free rates.

Table 3 shows the univariate and multivariate analysis results of age, stone burden, and the presence of HT. In multivariate analyzes, age and the presence of HT were found to be significant independent risk factors associated with hemoglobin decline (p<0.001, p=0.027). In the ROC analysis, area under the curve values were found as 0.885, 0.558, and 0.610 for age, HT, and stone burden, respectively (Fig. 1).

Discussion

Although PNL is the standard treatment method for large and complex kidney stones, potential complications pose a risk.[1] The main ones are fever, urinary tract infection, septicemia, renal colic, and bleeding requiring blood transfusion.[13] In the multicenter CROES study; the data from 5803 patients, who had undergone PNL surgery, were examined

Table 3. Univariate and multivariate analysis to determine the predictors of hemoglobin decrease

	Univariate			Multivariate		
	Exp (B)	95% CI	p	Exp (B)	95% CI	p
Age	0.841	0.801–0.883	0.000	0.840	0.799–0.882	0.000
Hypertension	3.014	1.117–8.134	0.029	3.781	1.168–12.247	0.027
Stone Burden	1.000	0.999–1.000	0.015	1.000	0.999–1.000	0.234

CI: Confidence interval.

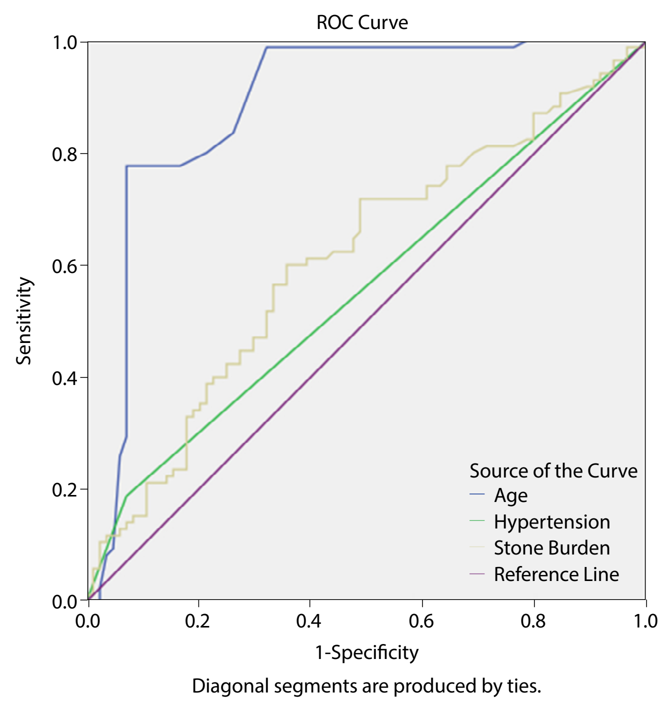

Figure 1. Receiver operating characteristic curve analysis of predictors of hemoglobin decrease.

and it was found that ASA scores, stone burden, and operative times were associated with the risk of requiring transfusion.[14] Similar to this result, in our study, it was found that stone burden and operation time were positively correlated with the amount of bleeding. In the CROES study; the overall perioperative complication rate was 20.5%, Grade 1 complication rate was 11.1%, Grade 2 was 5.3%, Grade 3 was 3.6%, Grade 4 rate was 0.5%, and Grade 5 rate was 0.03% after PNL.[14] Consistent with the results of the CROES study; in our study, Clavien 3a and Clavien 3b complications were observed at rates of 5.3% and 1.7%, respectively. No Grade 4 or Grade 5 complications occurred in our patient series. Complications were more severe and occurred more frequently in Group 1 compared to Group 2.

The need for transfusion, which is one of the most important complications secondary to PNL, varies from 1% to 10.8% in several studies.[5,15] The reason for that difference may be the use of diverse transfusion indications across different clinics. In our clinic; the decision for transfusion was made if symptomatic anemia, a postoperative hemoglobin reduction by more than 4 g/dl, or a hemoglobin level of <8 g/dl occurred. In a global study by Yamaguchi et al., the incidence of severe bleeding after PNL was found to be 9.4%.[16] While a conservative approach is sufficient in most of such bleeding cases, selective arterioembolization is required due to severe bleeding in frequencies ranging from 0.6% to 2.6%.[4,15] When conservative methods are inadequate such as clamping the nephrostomy catheter, giving hydration support, hemostatic drugs, and blood transfusion; arterial embolization is recommended as a safe method.[17] In our study, selective arterioembolization secondary to bleeding was applied to two of 169 patients in total, and the rate was 1.18% and it is compatible with the literature. In both of these patients; the procedure was curative, hemodynamic stability was achieved without the need for further treatment and transfusion, and hemogram decline stopped.

In the univariate and multivariate analyses in our study, age was found to be associated with higher magnitudes of hemoglobin reductions after PNL. Similarly, Keoghane et al. found in their study that age and operative times were associated with an increased risk for receiving transfusions after PNL.[7] For elderly patients, reduced ability to repair injury may be a possible mechanism for increased blood loss.[18] Today, in parallel to the increase in life expectancy, the elderly patient population with stone disease is growing. Changes in cardiovascular reserves in elderly patients make such patients less tolerant of serious stressors such as perioperative bleeding.[19] Decrease in body reserve and comorbidities are always a concern in the application of invasive treatment methods in elderly patients. However, well-controlled comorbidities do not increase the risk of surgery; PNL can be safe in elderly patients and gives a high stone-free rate.[20] In this respect, age is an important factor to be considered in evaluating patient eligibility and our study results support the association of higher age with high magnitudes of reductions in hemoglobin levels.

The previous studies reported that DM and HT are individual risk factors for bleeding due to possible atherosclerosis.[5,21,22] Furthermore, DM affects the entire vascular system, causing microangiopathies and increased tendency for bleeding.[3] In univariate analyses in their study, Akman et al. found out that DM and HT were correlated with decreased levels of hemoglobin. The multivariate regression analysis revealed that DM is an independent risk factor for bleeding, but it was found out that HT did not have a statistically significant effect on the total quantity of blood loss.[5] In their study, Kukreja et al. found out that there was not a significant relationship between HT and bleeding, but DM was found out to be a predictive factor for bleeding.[21] In their meta-analysis, Li et al. examined data from 10194 patients, who underwent PNL, and severe hemorrhagic complications were recorded in 142 of these patients.[22] They found out that risk factors for bleeding requiring selective arterioembolization included urinary tract infections, DM, the number of access, the type of the stone and HT. There was a significant difference in the first four of them, but not in HT. Our study did not found DM as an significant risk factor for bleeding, but it differs from the literature by showing that HT is an important risk factor for post-PNL bleeding. However, it was determined that the CCI score and the ASA score closely associated with these comorbidities were not variables affecting post-PNL bleeding.

There are several studies in the literature indicating that stone burden is a risk factor for bleeding.[21,23,24] The ultimate goal of PNL is to achieve the stone-free status to eliminate the obstruction and preserve kidney functions; requiring access to the whole calyceal system. However, maneuvers for achieving access to the calyceal system may cause tears and injuries along calyces. Furthermore, increased stone burden is associated with longer operative times leading to increased risk for bleeding.[25] Srivastava et al. found in their study that the only parameter predicting blood loss after PNL was stone burden.[26] Staghorn stones and large stones cause increases in the number of maneuvers and access needed to completely clear the pelvicalyceal system from stone fragments. Moreover; the use of rigid nephroscopes to reach stones in different calyces may cause injuries to the renal parenchyma and necks of calyces, resulting in an increased risk of intraoperative bleeding. The use of flexible nephroscopes can reduce the need for transfusions and the risk of bleeding without affecting success rates.[5,6] Consistent with the literature, it has been confirmed in our study that stone burden and operative times are significant risk factors in PNL-related bleeding.

The role of previous ipsilateral surgery for urolithiasis is controversial in terms of its effects on bleeding. Some authors reported that such surgery was associated with less bleeding.[21,23] On the contrary; Yeşil et al. reported that the position of the kidney became fixed due to adhesions between the kidney and the surrounding tissue after open surgery, limiting the mobility of the kidney during surgery and increasing rates of calyceal laceration and associated increases in bleeding.[27] Furthermore, it has been reported that the distribution of vascular structures in the kidney becomes sparse and therefore the risk of vascular injury during PNL decreases as the grade of hydronephrosis increases.[25] In our study, variables, such as the grade of hydronephrosis and the history of endoscopic and open surgery, have been analyzed revealing that such variables are not risk factors for bleeding after PNL.

Although our study is compatible with the literature in terms of its results, it makes a difference from the previous studies by the fact that HT is found to be a significant risk factor for bleeding. In addition, our study includes a comprehensive examination of stone characteristics by evaluating three different stone complexity scores. The most important limitation of this study was the retrospective design and the small number of patients included in the study. In recent years, there have been developments in the technique of endoscopic stone surgery in our clinic, PNLs have mostly begun to be performed in the supine position, balloon dilatation has been abandoned, and thus tract size has gradually decreased. To ensure patient homogeneity, these patients were not included in the study, and this situation caused our patient population to be relatively small. Furthermore, the procedures were performed by more than one surgeon and it should be kept in mind that the experience of the surgeon is a factor that may affect the results.

Conclusion

In this study; advanced age, presence of HT, and high stone burden were found to be predictive of reductions in hemoglobin levels. Furthermore, a correlation of decreased hemoglobin levels was detected with operative times and occurrence of complications. Taking such risk factors into account in patient eligibility in endourology will provide benefits in reducing surgery-associated comorbidities.

Disclosures

Ethics Committee Approval: The study approved by the Bakırkoy Dr. Sadi Konuk Training and Research Hospital Ethics Committee (No: 2021/06).

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Conflict of Interest: None declared.

Authorship Contributions: Concept – M.E., D.N.O., A.I.T.; Design – M.E., A.H., S.S.; Supervision – None; Materials – T.K., A.H.Y., A.H., S.K.; Data collection &/or processing – D.N.O., S.K., S.S.; Analysis and/or interpretation – M.E., T.K., A.H.Y.; Literature search – A.H., S.K., S.S.; Writing – M.E., D.N.O.; Critical review – M.E., A.I.T.

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